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(19) (CA) **CANADIAN PATENT** (12)

(54) Pulverulent, Water-Dispersable Carotenoid Formulations
and their Preparation

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ABSTRACT OF THE DISCLOSURE:

Pulverulent water-dispersable carotenoid formulations in which the carotenoid is dissolved in an edible oil and the oil solution is in the form of small droplets are prepared by a process in which a carotenoid is rapidly dissolved in a volatile, water-miscible, organic solvent at from 50 to 240°C, together with from 1.5 to 20 times the weight, based on the carotenoid, of an edible oil, and an emulsifier, under atmospheric or superatmospheric pressure, the hydrophilic solvent component is transferred to the aqueous phase from the resulting molecular disperse solution by immediate mixing with an aqueous solution of a protective colloid at from 0 to 50°C, the hydrophobic oil phase which contains the carotenoid in solution being formed as the microdisperse phase, and the resulting two-phase mixture is freed from the solvent and the water in a conventional manner. These formulations are in particular useful for coloring food and animal feeds.

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Pulverulent, water-dispersable carotenoid formulations
and their preparation

The present invention relates to the conversion of carotenoids to a finely divided, pulverulent form, the carotenoid being dissolved in an edible oil and the oil solution being in the form of very small oil drops. This formulation is used in particular for coloring food and animal feeds.

The carotenoids constitute a group of colored pigments which have a yellow to red hue, occur widely in nature and impart a typical color to many foods. The most important members of this class of substances are β -carotene, β -apo-8'-carotenal, canthaxanthine and citranaxanthine. These substances which can be synthesized are important colorants for both the food and animal feeds industry and pharmaceutical technology, for example as substitutes for synthetic colorants, and are of interest, for example, because of their provitamin A activity.

Virtually all carotenoids are insoluble in water and also have only slight solubility in fats and oils. This limited solubility and the high sensitivity to oxidation prevent the relatively coarse-particled products obtained in the synthesis from being used directly for coloring food or animal feeds, since only a low color yield can be achieved and the substances in coarsely crystalline form are poorly absorbed. These effects which are disadvantageous when the carotenoids are used in practice are particularly evident in an aqueous medium, since most of them are completely insoluble therein.

Various methods have been described for improving the color yields and increasing the absorbability, all of which aim at reducing the crystallite size of the active ingredients and bringing it to a particle size range smaller than 10 μm . For example, according to Chimia 21 (1967), 329, β -carotene together with edible oil can be milled to a particle size of from 2 to 5 μm



under a nitrogen atmosphere in a colloid mill. According to Food Technol. 12 (1958), 527, the coating oil simultaneously protects the active ingredient from oxidation. A suspension obtained in this manner and containing up to 20 or 30% of active ingredient can successfully be used for coloring fats and oils since the low solubility is nevertheless sufficient to dissolve the crystals at the low concentration usually employed.

While oily or fatty systems can thus readily be colored with the pure crystalline substances, aqueous systems are virtually impossible to color with the said substances. Furthermore, because most of the carotenoids are completely insoluble in water, the pure carotenoids mixed with the food or with the animal feed are very poorly utilized by the human or animal organism. The carotenoids have very limited solubility even in organic solvents, such as alcohols and alkanes.

The desired coloring and absorption properties can only be achieved via the very finely divided state. A desirable particle size is smaller than 1 μ m, which can be achieved by milling only with damage to the active ingredient, if at all.

Processes which represent a certain amount of progress in comparison are known processes in which the active ingredient is dissolved in a water-immiscible solvent, preferably a chlorohydrocarbon, such as chloroform or methylene chloride, the solution is emulsified by homogenization in a gelatine/sugar solution, and finally the solvent is stripped off from the emulsion, the active ingredient being liberated in finely crystalline form. This process is described in Chimia 21 (1967), 329, German Published Application DAS 1,211,911 and German Laid-Open Application DOS 2,534,091. A finely divided powder is then obtained from the resulting suspension by removal of water.

However, the abovementioned process has the disadvantage that chlorohydrocarbons have to be used in

order to achieve a sufficiently high concentration of active ingredient in the emulsion phase. Complete removal of the chlorohydrocarbons, which is necessary for toxicological reasons, is technically difficult to achieve.

5 These disadvantages were overcome by the process of European Patent 65,193, in which a carotenoid is dissolved in a volatile, water-miscible organic solvent at from 50 to 200°C, if necessary under superatmospheric pressure, in less than 10 seconds, the carotenoid is immediately precipi-
10 tated in colloidal form from the resulting molecular disperse solution by rapid mixing with an aqueous solution of a swellable colloid at from 0 to 50°C, and the resulting dispersion is freed from the solvent and the dispersing medium in a conventional manner. The mean size of the solid carotenoid
15 particles produced by this method is less than 0.3 µm.

 In another process (cf. U.S. Patent 2,861,891 and Austrian Patent 202,273), a water-dispersable carotenoid formulation is obtained by preparing, at from 100 to 160°C, a supersaturated solution of the carotenoid in an edible
20 oil which is liquid at about 20-40°C, emulsifying this supersaturated solution in an aqueous, gelatinous material, and converting the emulsion in a conventional manner to small dry particles.

 If the dry powder is redispersed in warm water,
25 a cloudy, orange yellow emulsion is formed again. This can be used, for example, for coloring food. Important performance characteristics of these colorant preparations are solubility, hue, color strength, opacity and stability in the medium used (R.H. Bunnell, W. Driscoll and I.C. Bauernfeind, Food Technol. XII (1958), 1-81).
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 However, a spectrophotometric investigation of the finely divided carotenoid formulations produced by the stated prior art shows that, particularly at fairly high concentrations, for example $\geq 2\%$ of dry powder, the
35 extinction values at the band maximum of the tinctorially effective absorption bands in the visible spectral range are only 50% of the maximum values achievable in a true

solution. From the economic point of view, this is a considerable disadvantage since only 50% of the potential color strength of a carotenoid can be utilized, for example for coloring a food, and the dose of the colorant therefore has to be doubled in order to obtain the desired color strength. It is also known that the hue of a food colored with carotenoids is determined to a great extent by the particle size and the physical state (solid, solution). With the prior art products, the range of potential differences in the hue of a selected carotenoid is far from being exhausted. It is furthermore known that the biological absorption of water-insoluble active ingredients, for example after oral administration, is greatly influenced by the particle size and the physical state. The carotenoid preparations produced according to the prior art therefore do not satisfy the precondition for optimum biological absorption.

It is an object of the present invention to provide a process which makes it possible to prepare carotenoid formulations which do not have the stated disadvantages.

We have found that this object is achieved, according to the invention, if the carotenoid is rapidly dissolved in a volatile, water-miscible, organic solvent at from 50 to 240°C, preferably from 150 to 200°C, together with from 1.5 to 20 times the weight, based on the carotenoid, of an edible oil, and an emulsifier, under atmospheric or superatmospheric pressure, the hydrophilic solvent component is transferred to the aqueous phase from the resulting molecular disperse solution by rapid mixing with an aqueous solution of a protective colloid at from 0 to 50°C, the hydrophobic oil phase which contains the carotenoid in solution being formed as the microdisperse phase, and the resulting two-phase mixture is freed from the solvent and the water in a conventional manner.

The novel procedure utilizes the fact that the

solubility of the carotenoids in a solution of an edible oil in water-miscible solvents, which is very low at low temperatures increases substantially with increasing temperature, but, despite the high temperatures, a short residence time at elevated temperatures substantially prevents isomerization which affects the hue, the color strength and the biological activity. However, this was in contradiction to the fact that the isomerization which usually occurs on heating in hot oil is itself used to inhibit recrystallization in the drops of the emulsified oil phase when the temperature is reduced, the said recrystallization having an adverse effect on the hue and the color strength of the desired end product. It was therefore surprising that, in spite of suppressing the tendency to isomerization at elevated temperatures, and after cooling, the product obtained by the novel procedure contains the carotenoid, spectrophotometrically detectable, as a molecular disperse, supersaturated oil solution stabilized to recrystallization, in the form of submicroscopic oil particles, and, compared with prior art products, has up to 100% greater color strength coupled with a shift in the hue to previously inaccessible ranges. The photochemical stability of the hydrosols prepared by the novel process is superior to that of the products prepared according to the prior art by a factor of more than 5.

The carotenoids which can be used for carrying out the invention are the known, obtainable, natural or synthetic members of this class of compounds, which can be used as color-imparting materials, for example carotene, lycopene, bixine, zeaxanthine, cryptoxanthine, citranaxanthine, luteine, canthaxanthine, astaxanthine, β -apo-4'-carotenal, β -apo-8'-carotenal, β -apo-12'-carotenal, β -apo-8'-carotenic acid and esters of hydroxyl-containing and carboxyl-containing members of this group, for example the lower alkyl esters and preferably the methyl and ethyl esters. The compounds which have been readily

available industrially to date, such as β -carotene, canthaxanthine, β -apo-8'-carotenal and β -apo-8'-carotenates, are particularly preferred.

5 Water-miscible, heat-stable, volatile solvents containing only carbon, hydrogen and oxygen, eg. alcohols, ethers, esters, ketones and acetals, are particularly suitable for carrying out the novel process. Ethanol, n-propanol, isopropanol, butane-1,2-diol 1-methyl ether, propane-1,2-diol 1-n-propyl ether and acetone are preferably used.

10 In general, it is advantageous to use solvents which are not less than 10% water-miscible, have a boiling point of less than 200°C and/or contain less than 10 carbon atoms.

15 Suitable edible oils are oils which are liquid at from 20 to 40°C. Examples are vegetable oils, such as corn oil, coconut oil, sesame oil, peanut oil, soybean oil or cottonseed oil. Peanut oil is particularly preferred. Other suitable oils or fats are shortening, beef dripping and butter fat. The edible oils are generally used in an amount of from 1.5 to 20, preferably from 3 to 8, times the weight of the carotenoid, and the total oil content of the carotenoid formulation should not exceed 60% by weight if it is intended to prepare a dry powder.

25 Suitable protective colloids are any conventional protective colloids permitted in food and animal feeds; examples are gelatine, starch, dextrin, dextran, pectin, gum arabic, casein, caseinate, whole milk, skimmed milk, milk powder or mixtures of these. However, it is also possible to use polyvinyl alcohol, polyvinylpyrrolidone, methylcellulose, carboxymethylcellulose, hydroxypropylcellulose and alginates. For further details, reference may be made to R.A. Morton, Fast Soluble Vitamins, Intern. Encyclopedia of Food and Nutrition, Vol. 9, Pergamon Press, 1970, pages 128-131. To increase the mechanical stability of the end product, it is advantageous to add to the colloid a plasticizer, such as sugar or sugar

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alcohols, eg. sucrose, glucose, lactose, invert sugar, sorbitol, mannitol or glycerol. Minor amounts of methyl esters or propyl esters of p-hydroxybenzoic acid, sorbic acid and Na benzoate may also be added as preservatives.

5 The ratio of protective colloid, plasticizer and oil to carotenoid is in general chosen so that the resulting end product contains from 0.5 to 10, preferably from 2 to 5, % by weight of carotenoid, from 5 to 50% by weight of an edible oil, from 10 to 50% by weight of a protective colloid and from 20 to 70% by weight of a plasticizer, all percentages being based on the dry weight of the powder, as well as minor amounts of a stabilizer. The mean particle size of the oil phase present in the powder and supersaturated molecular disperse carotenoid is less than 0.3 μm , and the half width of the size distribution is less than 50%. The product contains virtually no oil particles having a particle size greater than 1 μm .

20 To increase the stability of the active ingredient to oxidative degradation, it is advantageous to add stabilizers, such as α -tocopherol, lecithin, tert-butylhydroxytoluene, tert-butylhydroxyanisole, ethoxyquine or ascorbyl palmitate.

25 They can be added to either the aqueous phase or the solvent phase but are preferably dissolved together with the colorants and the oil, in the solvent phase.

30 The novel process gives a viscous liquid which has a deep coloration and from which the solvent can be removed in a conventional manner depending on the boiling point, for example by distillation, under atmospheric or reduced pressure, or by extraction with a water-immiscible solvent. Preferably, however, the solvent is removed together with the water by spray drying or spray granulation.

35 The dry powder obtained can be redissolved in water with uniform fine distribution of the active ingredient in the particle size range $< 0.5 \mu\text{m}$. The

photochemical stability test shows that the resulting hydrosol of the active ingredient is extremely stable despite being finely divided.

5 If necessary, the microdisperse oil phase super-saturated with carotenoid can also be brought to a suitable pH and then flocculated together with the protective colloid and thus converted to a form from which the solvent and a major part of the dispersing medium can be removed in a simple manner by filtration or centrifuging. The co-
10 acervate thus obtained is then further dried in a conventional manner and converted to granules.

Specifically, the novel process is carried out as follows, for example using an apparatus as shown schematically in Fig. 1.

15 The apparatus is divided into parts I, II and III. Part II is the high temperature section, while in parts I and III the temperatures are less than 50°C.

In vessel (1), a suspension of the carotenoid together with the oil in the selected solvent in a concentration of from 2 to 20% by weight, based on the mixture,
20 with or without the addition of from 0.1 to 10% by weight of stabilizers, is initially taken. Vessel (2) contains the solvent without admixed carotenoid. The suspensions of active ingredient and the solvent are fed to the mixing chamber (7) via the pumps (3) and (4) respectively;
25 the mixing ratio can be predetermined by choosing the particular delivery of the pumps, and is selected so that, depending on the solvent and the residence time, the resulting carotenoid concentration in the mixing chamber is from 0.5 to 10% by weight, based on the solution. The
30 volume of the mixing chamber (7) is such that the residence time in (7) is preferably less than 1 second at the selected delivery of the pumps (3) and (4).

Before entering the mixing chamber, the solvent
35 is brought to the desired temperature by means of the heat exchanger (6), while the oil-containing suspension of active ingredient is kept at below 50°C by feeding it

via the thermally insulated line (5). As a result of turbulent mixing in (7) at from 50 to 240°C, preferably from 150 to 200°C, the active ingredient goes into solution, and, after a short residence time, preferably less than 1 second, the resulting solution passes via (8) into the second mixing chamber (11), in which, by admixing an aqueous protective colloid/plasticizer solution via pump (9) and feed line (10), the molecular disperse carotenoid solution is divided into a two-phase mixture with formation of a microdisperse oil phase containing the active ingredient in supersaturated solution and a homogeneous, aqueous phase containing the water-miscible solvent. The microdisperse two-phase mixture is then discharged via line (12) and the pressure relief valve and fed to the stock vessel (14). To obtain a very high concentration of active ingredient, the dispersion can be circulated via the suction line (15).

If the pressure relief valve (13) is set at above one bar, it is even possible to use solvents at temperatures above their boiling point (under atmospheric pressure) in the novel process.

A pulverulent preparation can be obtained from the dispersion in a conventional manner, for example as described in German Laid-Open Application DOS 2,534,091, by spray drying or by spray cooling or by coating the particles, separation and drying in a fluidized bed.

For spray drying, the dispersion is either first freed from the solvent by distillation, preferably under reduced pressure, or by extraction with a water-immiscible solvent, or the entire mixture is spray-dried and water and solvent are stripped off together in the spray tower in this manner.

The carotenoid powder is obtained in either dry or free-flowing form at the bottom of the spray tower. In some cases, it may be advantageous additionally to carry out complete drying in a fluidized bed. Instead of preparing the powder formulation by spray drying, it

carotenoids already finely distributed in the water/oil/solvent dispersion into powder form.

5 A known and equally suitable method comprises, for example, emulsifying the dispersion freed from the solvent with liquid paraffin, cooling the mixture, separating the liquid paraffin from the coated carotenoid particles, washing the resulting carotenoid preparation with naphtha and drying the preparation in a fluidized
10 bed.

In the novel procedure, it was particularly surprising that the use of the stated water-miscible solvents mixed with an edible oil which may additionally contain emulsifiers, such as ascorbyl palmitate, mono-
15 and diglycerides, esters of monoglycerides with acetic acid, citric acid, lactic acid or diacetyltartaric acid, polyglycerol fatty acid esters, sorbitan fatty acid esters, propylene glycol fatty acid esters, stearyl 2-lactylates or lecithin, permits the preparation of highly
20 supersaturated solutions in which, in spite of suppression of the trans-cis isomerization, no recrystallization of the carotenoid takes place within the submicroscopic oil drops supersaturated with active ingredient in the microdisperse oil phase, after the phase separation induced by turbulent mixing with the aqueous protective
25 colloid solution, even during removal of the volatile solvent, for example by distillation or spray drying, and after cooling.

It is furthermore surprising that admixing of the
30 solvent-containing oil solution of the carotenoids with the aqueous protective colloid solution induces phase separation during which the disperse oil phase is obtained in the form of extremely small particles, as cannot be obtained by mechanical homogenization. This finely
35 dispersed state of the oil phase supersaturated with active ingredient is also maintained during removal of the volatile solvent, for example by spray drying. It is

5 easily possible to obtain preparations in which the major fraction in the oil phase has a particle size of 0.2 μm , without particles of active ingredient larger than 1 μm simultaneously being present. The absorption spectrum of such carotenoid preparations shows the band form and extinction typical of the molecular disperse solution of a carotenoid in an edible oil, even after spray drying and redissolution in an aqueous medium.

10 The Examples which follow illustrate the novel process.

EXAMPLE 1

5 5 g of β -trans-carotene are suspended in 240 g of a solution of 4 g of ascorbyl palmitate, 5 g of α -tocopherol and 20 g of peanut oil in isopropanol, the pressure relief valve (13) is set at 25 bar and the said
15 suspension is mixed in mixing chamber (7) with 360 g of isopropanol which has been heated to 225°C in heat exchanger (6). The suspension is metered at 2 l/h and the solvent at 3 l/h, and the residence time in mixing chamber (7) is 0.35 second. The molecular disperse solution
20 formed at 190°C is then fed to mixing chamber (11), in which turbulent mixing with 4,000 g of an aqueous solution of 60 g of gelatine and 90 g of sucrose, brought to pH 9 with 1N NaOH, at a metering rate of 27 l/h results
25 in phase separation with formation of a microdisperse oil phase which contains the β -carotene in the form of a supersaturated solution. A microdisperse two-phase mixture having a yellow hue and a temperature of 50°C is obtained in collecting vessel (14). Particle size analysis by proton correlation spectroscopy gives a mean particle size of the oil phase of 210 nm and a distribution width of $\pm 40\%$.

30 Removal of the solvent under reduced pressure at 50°C in a distillation apparatus gives a viscous liquid which can be converted to a stable, water-soluble dry powder by spray drying. The β -carotene content of this
35 dry powder is 2.4% by weight.

Redissolving the dry powder in cold water gives a yellow solution in which the oil phase is again present as a microdisperse phase having a particle size of 220 nm +30%.

5 Spectrophotometric investigation of this solution shows the β -carotene band form typical of a molecular disperse solution (Fig. 2a). In contrast, the prior art gives a product which, for the same concentration of active ingredient in aqueous solution, gives an absorption
10 spectrum showing the typical curve of a β -carotene solid-state spectrum (Fig. 2b). The ratio of the extinction values at the band maxima is 2.1. Hence, the novel process gives a preparation which has more than twice the color strength of a prior art preparation.

15 In spite of the extremely finely divided nature and the high color strength, the hydrosol exhibits excellent stability in the photostability test. Under standardized irradiation conditions, a loss of active ingredient of 10% is recorded during an irradiation time
20 of 270 minutes. In the case of products having a β -carotene content of 2.4% and prepared according to the prior art, a loss of active ingredient of 10% is observed under the same irradiation conditions after only 50 minutes.

25 EXAMPLE 2

A two-phase mixture is obtained as described in Example 1, but with the use of 10 g β -trans-carotene, 8 g of ascorbyl palmitate and 40 g of peanut oil; in the said mixture, the oil phase supersaturated with β -carotene
30 is in the form of submicroscopic droplets having a mean particle size of 249 nm +52%.

The dry powder obtained by spray drying contains 5% of active ingredient and, after redissolution in water, gives a hydrosol having a mean particle size of 289 nm
35 +54%. Compared with the prior art product, the extinction ratio at the band maximum is 1.8.

EXAMPLE 3

5 A dry powder is obtained as described in Example 1, but with the use of 5 g of canthaxanthine; after redissolution in water, the said powder gives a hydrosol having a mean particle size of 191 nm $\pm 42\%$. The extinction at the band maximum at $\lambda = 478$ nm is 90% of the theoretical maximum value, whereas prior art products give extinction values which are no more than 50% of the theoretical values.

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EXAMPLE 4

A dry powder is obtained as described in Example 1, but with the use of 60 g of gum arabic as a protective colloid; after dissolution in water, the said powder gives a hydrosol having a mean particle size of 359 nm $\pm 42\%$.

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A pulverulent, water-dispersable carotenoid formulation in which the carotenoid is dissolved in an edible oil and the oil solution is in the form of small droplets which are dispersed as a pulverulent matrix, obtainable by rapidly dissolving a carotenoid in a volatile, water-miscible, organic solvent at from 50 to 140°C, together with from 1.5 to 20 times the weight, based on the carotenoid, of an edible oil, and an emulsifier, under atmospheric or superatmospheric pressure, then immediately mixing with an aqueous solution of a protective colloid at from 0 to 50°C and thus transferring the hydrophilic solvent component to the aqueous phase, the hydrophobic oil phase which contains the carotenoid in solution being formed as the microdisperse phase, and freeing the resulting two-phase mixture from the solvent and the water.

2. A process for the preparation of a pulverulent water-dispersable carotenoid formulation in which the carotenoid is dissolved in an edible oil and the oil solution is in the form of small droplets, wherein:

a carotenoid is rapidly dissolved in a volatile, water-miscible, organic solvent at from 50 to 240°C, together with from 1.5 to 20 times the weight, based on the carotenoid, of an edible oil and an emulsifier, under atmospheric or superatmospheric pressure, so as to form a molecular disperse solution;

the so formed molecular disperse solution is mixed with an aqueous solution of a protective colloid at from 0 to 50°C, the hydrophilic solvent component contained in said molecular disperse solution being then transferred to the aqueous phase of said aqueous solution, the hydrophobic oil

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phase which contains the carotenoid in solution being then formed as the micro-disperse phase; and

the two-phase mixture that is so obtained is freed from the solvent and the water.

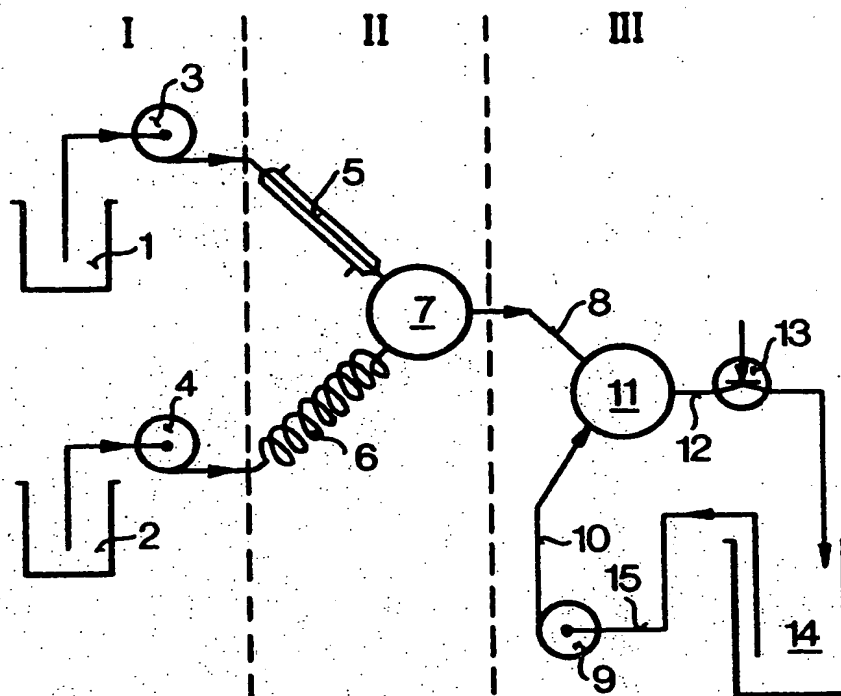
3. A process as claimed in claim 2, wherein the carotenoid is dissolved at from 150 to 200°C.

4. A process as claimed in claim 2, wherein the carotenoid is dissolved in less than 1 second, and the resulting solution is immediately cooled by mixing with the aqueous solution of the protective colloid and converted to the microdisperse two-phase mixture.



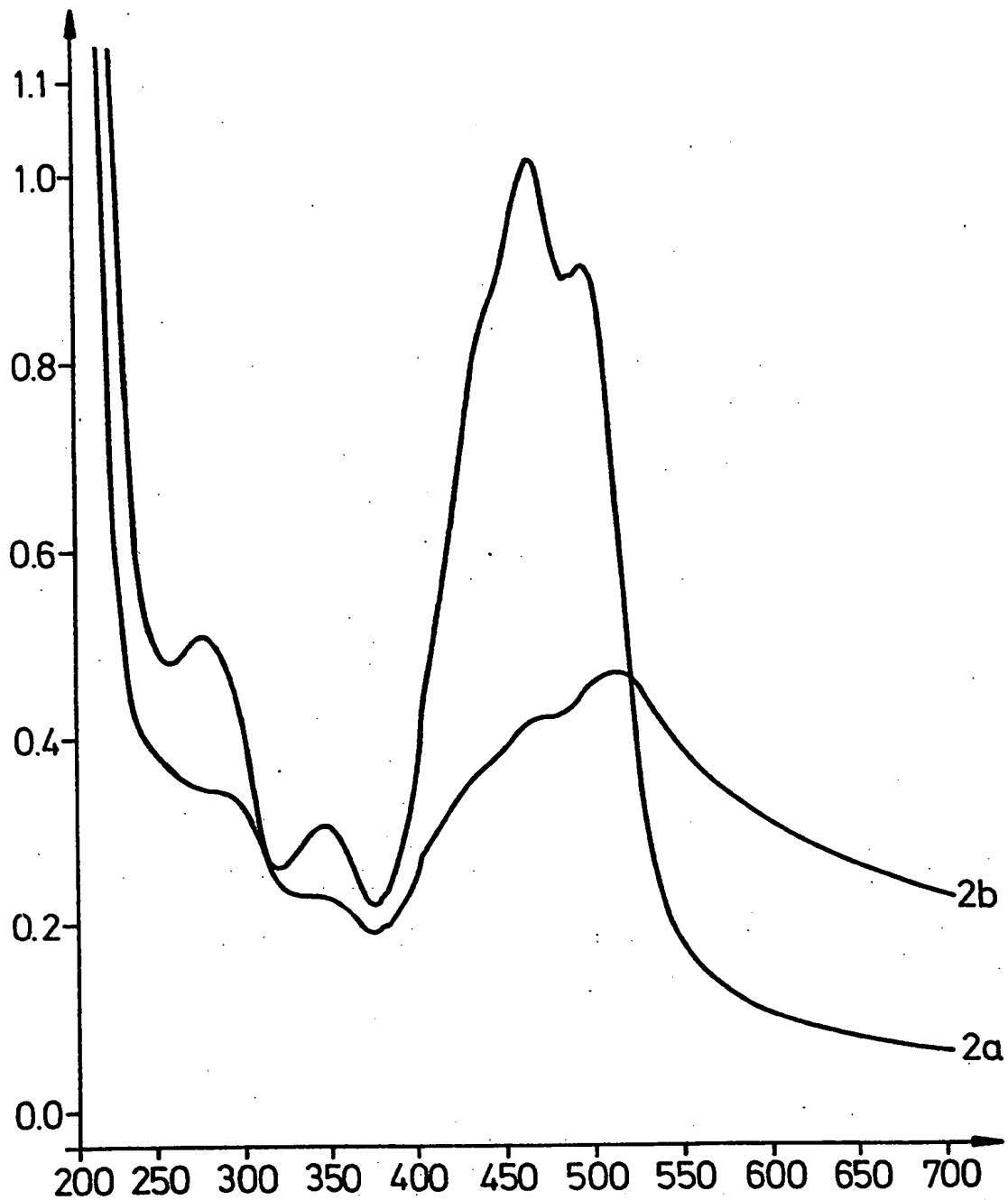
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FIG. 1



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FIG. 2



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